

latent syphilitic. Chesney and Kemp showed that a rabbit which had been treated for an old infection and still had positive reaction was not infectious when its glands and organs were inoculated into a healthy rabbit. Walserlin and Carroll, on the other hand, while using rabbits showed that in recent cases the positive Wassermann existed when there were active lesions and became negative when the active lesions subsided. The positive Wassermann then indicates that syphilis is present and in old and treated cases may mean that spirochaetae are hibernating in inaccessible parts of the body and that the individual may live his normal expectancy unless something happens to disturb the balance. We all know that there are patients in whom the infection is old, who have a positive Wassermann and in whom no treatment or combination of treatment can make negative. In a series of this character who were treated at the New York Hospital for an average period of forty months only 56 per cent were made negative, so don't get discouraged if some of your old patients still have a positive Wassermann. *Above all do not hasten a fatal issue by too intensive treatment.*

Most syphilitic patients are led to believe that their great cross is a plus Wassermann. They think themselves cheated if after a few doses of salvarsan it still remains positive. They even become syphilophobiac simply because of the 4 plus Wassermann. As soon as it becomes negative they say, "At last I am cured." Some physicians even encourage or support this view, but if they would stop to think they would realize that a negative Wassermann does not mean a cure. If the Wassermann reaction is not a reliable index of cure, what are we to rely upon? Physical examination surely will not definitely determine whether or not a cure has been effected. Warthin cites five cases where the Wassermann of both parents was negative and syphilitic babies were born, so therefore it seems fair to conclude that there is no definite criterion as to the cure of syphilis.

The important conclusion to be drawn, then, is not when a syphilitic patient is cured, for that is sometimes a question of academic interest and no one can tell definitely. The real question is when and in what amounts and for how long treatment should be given. Most early lesions can be made harmless, latent or cured, but the period during which treatment should be given should be longer than is usually advised and an occasional survey should be made of the individual for many years afterward. Patients with early lesions require, as a rule, from one to three years' treatment, and most of those with late lesions should have nearly as long a course of treatment, but the doses should be smaller. Nerve syphilis may require some form of intraspinal or malarial treatment, but that is another story. Late heart and organic types should have an entirely different procedure. Arsenic is often injurious to them and should be preceded by iodide and mercury and then small doses of arsenic preparations given carefully. The treatment of all patients should be modified by their conditions and an annual examination should be made for many years to see if any signs of syphilitic degeneration can be detected.

Special Article

HYPOPHYSIS VERSUS HYPOTHALAMUS

By H. LISSER *

THE writer prefaced a chapter on the pituitary body with the following quotation:

"Thus do interpretations throng and clash, and neatly equal the commentators in number. Yet possibly each one of these unriddlings, with no doubt a host of others, is conceivable, so that wisdom will dwell upon none of them very seriously" (from Jurgen, by Cabell).

This quaint bit of irony, to some extent at least, reflects the present status of pituitary problems.

Several years ago (about 1920) Camus and Roussy declared war on the then prevalent conceptions of pituitary function. They seized upon a relatively unexplained region, the hypothalamus, not far from the hypophysis, and established their base of operations in the tuber cinereum. They contented themselves, modestly at first, by stealing the diabetes insipidus syndrome from pituitary ownership, which they produced experimentally in dogs by injuring the tuber cinereum (the hypophysis remaining intact). Before long they made another invasion and laid claim to proprietary rights over Frölich's adiposogenital dystrophy which had been in possession of the pituitary since Frölich's first description in 1901. They had reproduced this clinical complex in dogs by traumatizing the hypothalamus (again, supposedly, without harm to the hypophysis).

Meanwhile the pituitary body was torn asunder. Originally separated into two parts, a front and a behind, further investigation produced further divisions: a pars intermedia, and a pars tuberalis (surrounding the infundibular stalk and extending up into the floor of the third ventricle). The respective guardians of these several lobes claimed certain characteristics, powers and functions for their pet portions which conflicted or trespassed one upon the other. In the confusion such matters as skeletal growth, genital disturbances, obesity, emaciation, polyuria and polydipsia, and interrelations with other ductless glands (especially the thyroid, suprarenals, and gonads) became involved and disputed. Laborious classifications of the several functions of the several lobes, whether clinical, pathological or physiological, did not serve to clarify the confusion. Laudable efforts they were, but their orderliness did not rest on sufficiently secure foundations.

The attacks of Camus and Roussy, aided and abetted by Bailey and Bremer, Houssay, Leschke, Curtis and others, caused dismay in the ranks of the

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traditional hypophysists and some forsook their pituitary allegiance, fleeing over the pituitary stalk into the depths of the hypothalamus to rally round the new genitotrophic centers. The vanguard of the hypothalamists became so radical in their views that they refused to admit that the pituitary exercised any function whatsoever. Its indispensability to life had already been challenged (Dandy, etc.); now even its functional significance was scorned.

It was fortunate in this turbulent state of affairs that two leaders arose, one a veteran of adrenal fame, Professor Abel of Johns Hopkins, the other, Professor Evans of the University of California. The former took charge of the posterior portion of the hypophysis, while the latter concentrated his efforts mainly on the anterior lobe. They entrenched themselves within the sella turcica and speedily regained some of the ground which seemed to have been lost.

Professor Abel isolated a tartrate from the pars posterior and pars intermedia, not yet of entire chemical purity, but of extraordinary potency being 1200 times as powerful as the acid phosphate of histamin, heretofore the strongest smooth muscle stimulant known. Abel and Geiling observed "that the floor of the third ventricle in the immediate vicinity and inclusive of the tuber cinereum contains a blood-pressure-raising and oxytocic substance quite indistinguishable from that present in the posterior lobe of the hypophysis." In ablation of the hypophysis this accessory tissue cannot be removed; it could still perform the function of the posterior lobe and thus prevent a diabetes insipidus. Abel,¹ therefore, is disinclined to accept the negative position of Camus and Roussy "in regard to the function of hypophyseal tissue."

Evans² and coworkers prepared a fresh bovine anterior lobe fluid which had remarkable growth-inducing properties. Repeated injections of this fluid into normal rats produced gigantism, and a replacement therapy with this extract, in rats dwarfed by an early hypophysectomy, stimulated normal growth and repaired the pituitary deficiency. This work was so convincing that Roussy and Bremer have retracted somewhat from their complete skepticism of pituitary function and have granted that "the rôle of the anterior pituitary in skeletal growth is well established."

P. E. Smith, who, it will be remembered, performed the delicate hypophysectomies on tadpoles and who was able to repair the resultant disabilities (a slowed growth rate, suprarenal cortex and thyroid atrophy, pigmentary changes and failure to metamorphose) by injections of Evans' bovine anterior lobe fluid, proceeded to collaborate with Evans in experiments on the rat. At first he produced pituitary deficiency by what he now calls a "crude method," the injection of chromic acid into the gland. Dwarfism not only resulted from this operation, but also significant degenerations in the thyroid, suprarenals, and gonads. As related, the dwarfism was corrected by injections of Evans' anterior lobe fluid, but late reports indicate that the secondary

changes in the other endocrine organs cannot be repaired by this hormone.

Smith,³ now at Stanford University, sheds further light on these problems in a recent paper. He has devised a new method of pituitary ablation in the rat. The gland is sucked out through a glass cannula with negative pressure, after the ventral surface has been exposed. The dural sheath of the gland, dorsally, and the pituitary stalk are left intact, which prevents the escape of cerebrospinal fluid. The hypothalamus is not injured. In another series of rats the pituitary has been carefully avoided while lesions have been made in the hypothalamus. Smith claims that "these two operations, pituitary ablation and tuberal injury, produce distinct and characteristic syndromes." The hypophysectomy syndrome consists chiefly of: "an almost complete inhibition in growth in the young animal, and a progressive loss of weight (cachexia) in the adult; an atrophy of the genital system with loss of libido sexualis, and in the female an immediate cessation of the sex cycles; an atrophy of the thyroids, parathyroids and suprarenal cortex; and a general physical impairment." This experimental syndrome corresponds closely to the clinical complex, hypophyseal cachexia (Simmond's disease), of which a few cases have been recorded (mostly in the German literature), characterized as a rule by a chronic course, progressive emaciation and fatal termination; the only lesion at necropsy being a complete atrophy of the pituitary body. Smith has been successful in restoring his hypophysectomized rats to normal, both male and female, young and adult, not only in respect to growth but also as regards gonadal function and repair of thyroid, parathyroids and suprarenals—by a replacement therapy consisting of daily intramuscular homotransplants of living hypophyseal tissue.

In contrast to the foregoing, injury to the hypothalamus produced adiposity and genital atrophy, an experimental state corresponding to what is generally referred to, in the human, as Frölich's syndrome (dystrophia adiposogenitalis), although the original case of Frölich's, a boy with pituitary tumor, also showed skeletal undergrowth. It must be admitted, however, that this relatively common clinical disorder is but rarely attended by skeletal retardation. These clean-cut experiments of Smith are rather a shock to those who cling to the idea of a pituitary obesity, and who believe they have helped to reduce such adiposity and restore menstruation by the administration of pituitary extracts. This tuberal obesity may be extreme, biochemical examination disclosing that 50 to 75 per cent of the total weight is fat. Injection of Evans' anterior pituitary extract has no effect on the adiposity or genital dystrophy, but Smith does not state whether transplants of living pituitary tissue are likewise ineffectual.

It would seem, therefore, that the pituitary body has not entirely lost its place as an endocrine organ, but that some of the metabolic derangements formerly ascribed to it (obesity, polyuria, polydipsia, etc.) may be due to disturbances of so-called genitotrophic centers in the hypothalamus. But the end is not yet, and a "prepared open mind" is the safest

1. Bull. of the Johns Hopkins Hospital, 1926, 38, 1-32.

2. The Function of the Anterior Hypophysis, Harvey Lecture, 1924.

3. Journal American Medical Association, 1927, 88, 158-161.

attitude. In other words, one may be permitted a certain conservatism sitting on the fence, as it were, the fence in this case being the pituitary stalk, with one foot in the hypophysis and the other in the hypothalamus. Such a compromised position has been adopted by Biedl, who offers a theory which Solis-Cohen described as "more than highly plausible," even "seductive." For such disorders as Frölich's syndrome and diabetes insipidus he would postulate three pathogenetic possibilities: (a) disease or defect of the hypophysis (pars intermedia or posterior lobe) with deficient hormone; (b) obstruction of an assumed pathway (for instance by tumor or internal hydrocephalus) preventing a normal amount of hormone from reaching or energizing certain metabolic and genitotrophic centers in the hypothalamus; and (c) cerebral lesions of these alleged trophic centers themselves, such as tumor, traumatism, tuberculosis, syphilis or encephalitis, or congenital defect.

This platform is certainly broad enough for all parties to the controversy, probably too broad. Meanwhile many of us as interested spectators can take seats on the pituitary stalk and watch the struggle between hypophysis and hypothalamus.

CLINICAL NOTES, CASE REPORTS AND NEW INSTRUMENTS

STAPHYLOCOCCUS SEPTICEMIA

CASE REPORTS

By ALFRED C. REED AND FRANK E. STILES *

CASE 1—E. E. This patient, a girl aged 14, was admitted complaining of deep pain in the right thigh. She stated that as she was getting up from the supper table four days before admission she experienced a severe sharp pain in her right thigh about halfway between the knee and the hip. Previous to this she had been feeling well, doing her daily duties and playing with other children with no discomfort whatever. The pain increased, she remained in bed four days, and as there was no improvement sought medical relief.

Past History—Had measles at 3; tonsillitis followed by tonsillectomy at 10; mumps at 13; and influenza ten months ago. Last year she had several generalized crops of boils, the last of which disappeared six months ago.

Physical examination showed a well-developed and well-nourished girl with flushed, dry skin, lying in a fixed position, although not evidently in great pain. The anterior cervical glands were somewhat enlarged. Her extremities presented the only important abnormalities. There were many small maculo-papular lesions on both

legs. Some small old scars were seen on the legs, residua of the boils of six months previous. Definite point tenderness was elicited over the upper third of the right femur, and she cried out in pain upon flexion of the leg on the thigh.

Laboratory work on admission showed a red blood count of 4,000,000 with 70 per cent hemoglobin, and a white count of 8600 with a normal differential count. The urine was normal. The Wassermann was negative.

Her temperature was of a septic type, high in the daytime and low at night, ranging from 105 to 100 F. Raised, swollen, painful areas similar to that on the thigh appeared day after day in the following order: the left thigh, left leg, right hand, sternum, left arm, left hand, right arm. Three blood cultures taken on successive days were all positive for staphylococcus aureus. The red cell count ranged from 4,000,000 on admission to 2,600,000 the day before death. The white count ranged from 9000 to 5000, the latter being the last taken. The polymorphonuclear content never rose above 76 per cent. X-rays of the right femur and hip were negative. Except for slight delirium on the second day when her temperature was 105, she was mentally clear till the morning of her death, and except for the painful swellings already referred to and a sallow, jaundiced appearance to the skin, the physical findings remained the same until two days before death, when bronchopneumonia appeared in both lungs. Death came on the eleventh day after admission.

Treatment—Hot epsom salt compresses were used on the painful areas, with salicylates and codein sufficient to control pain. Daily doses of 1 per cent gentian violet were given intravenously for five days in these respective amounts: 1-15 cc., 2-15 cc., 3-20 cc., 4-20 cc., 5-25 cc.

Autopsy—Every part of the body examined was found saturated with pus. Multiple abscesses exuding pus were found in the soft tissues under the skin at the site of the swollen areas referred to above. Abscesses were also found in the mediastinum, lungs, pericardium, heart, spleen, liver, and kidneys. Smears from these tissues showed numerous small clusters of staphylococci, and microscopical study of the organs disclosed innumerable abscesses.

The pathological diagnoses were: purulent dermatitis, purulent pericarditis with effusion, acute myocarditis, empyema, and miliary abscesses of the spleen, kidneys, and liver. The cause of death was staphylococcus septicemia, probably resulting from her previous boils.

Comment—This case is typical throughout. The portal of entry was apparently an earlier furunculosis, a source which almost invariably leads to a fatal termination. The metastatic abscesses were unusually numerous and widely distributed. The low white count measured the fulminating type of infection. The absence of osteomyelitis is worthy of note.

CASE 2—R. C. This patient was seen by one of us (A. C. R.) on January 20, 1926, when his complaint was of a boil on the upper lip, with several enlarged glands below the jaw. He had chronically infected tonsil stumps, otherwise was normal. Mercurochrome was applied to the boil after free drainage. Nine days later he had a crop of small pustulations on the face, the anterior cervical glands were much enlarged and there was a painful, raised, tender, reddish spot on each knee. Temperature was 99.6 F. on February 1, similar spots were distributed well over the lower extremities, and the face and neck. On February 6, the lesions were maximal, temperature ranged between 99.4 and 101.6. Smears from the suppurating skin lesions showed pure staphylococcus and the white blood count was 10,900 with 73 per cent polymorphonuclears. The patient felt quite well. Blood cultures were not made. Treatment with mercurochrome applications and epsom salt compresses did not limit or control the skin lesions. Finally gentian violet, 1 per cent solution, was given intravenously in a 30 cc. dosage. The temperature came to normal, no new lesions appeared and no recurrence up to March 10, 1927.

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